

## REMARKS

Applicants wish to thank Examiner Epps-Ford for the courteous personal interview conducted on November 2, 2005 to discuss the issues raised by the Office Action mailed October 4, 2005. Claims 15-19 are withdrawn without prejudice or disclaimer. Claims 1, 4, 5, 8-12, 20, and 28 have been amended. Support for the claim amendments can be found throughout the specification. Claims 2, 3, 6, 7, 14, and 21-27 are canceled. Newly introduced Claims 29-39 find support throughout the specification. Support for the use of "start codon region" in amended Claim 1 and nucleotide ranges in newly introduced claims 29-32 can be found on page 9, lines 10-14. Accordingly, no new matter has been added by way of these amendments.

Following entry of the amendments submitted herewith, Claims 1, 4, 5, 8-13, 20, 28, and 29-39 are presented for examination. Reconsideration of the currently presented claims in view of the amendments and comments set forth herein is respectfully requested.

### *Discussion of Rejection Under 35 U.S.C. §112, first paragraph*

The Examiner rejected claims 1, 11, 20 and 28 under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement. Applicants respectfully disagree. However, solely in an effort to advance prosecution, Applicants have amended claims 1, 11, and 20 to replace "non-cleaving" with "non-catalytic" and to replace "compound" with "oligonucleotide compound". As agreed during the interview of November 2, 2005, this amendment obviates the rejection and therefore Applicants respectfully request that it be withdrawn.

### *Discussion of Rejection Under 35 U.S.C. §102*

The Examiner rejected claims 1, 2, 4, 5, 11, 12, 14 and 20 under 35 U.S.C. §102(b) as being anticipated by Tang et al., who allegedly disclose an antisense compound that is 20 nucleotides in length targeting nucleotides 129 through 148 of SEQ ID NO: 3. The Examiner argues that the structure of the antisense compound disclosed by Tang et al. meets the structural limitations recited in the instant claims.

Applicants maintain that claims 1, 2, 4, 5, 11, 12, 14 and 20, as presented in their response of June 15, 2005, are novel over Tang et al. However, in an effort to advance prosecution of the instant application, independent claims 1 and 11 have been amended such that non-catalytic oligonucleotide compounds targeted to the start codon of SEQ ID NO: 3 are excluded from the genus of non-catalytic oligonucleotide compounds encompassed by these claims. As defined by the instant specification, the “start codon region” encompasses from about 25 to about 50 contiguous nucleotides in the 5’ or 3’ direction from a translation initiation codon (see page 9, lines 10-14). Therefore, the portion of SEQ ID NO: 3 targeted by the antisense compound allegedly disclosed by Tang et al. is encompassed by the term “start codon region”. Accordingly, Tang et al. do not disclose the structural limitations of claims 1 or 11. Nor would the claimed non-catalytic oligonucleotide compounds be obvious in view of Tang et al., as one of ordinary skill in the art, upon reviewing the disclosure of Tang et al., would not have a reasonable expectation of success in making the oligonucleotide compounds as claimed, as further described below. Accordingly, in view of these amendments, Applicants respectfully request that the rejection of claims 1, 2, 4, 5, 11, 12, 14 and 20 under 35 U.S.C. §102(b) be withdrawn.

*Discussion of Rejection Under 35 USC § 103*

The Examiner rejected Claims 1, 2, 4-14, 20, and 28 under 35 U.S.C. 103(a) as being unpatentable over Tang et al. in view of Cowsert (U.S. Patent No. 5,945,290). Applicants respectfully disagree.

To establish a *prima facie* case of obviousness a three-prong test must be met. First, there must be some suggestion or motivation, either in the references or in the knowledge generally available among those of ordinary skill in the art, to modify the reference. Second, there must be a reasonable expectation of success found in the prior art. Third, the prior art must reference must teach or suggest all the claim limitations. *In re Vaeck*, 947 F.2d 488 (Fed. Cir. 1991).

The Examiner argues that “one of ordinary skill in the art would have been motivated to modify the antisense compound and compositions of Tang et al.” with the teachings of Cowsert in the design of the instant invention.

Applicants maintain that claims 1, 2, 4-14, 20 and 28 are nonobvious in view of the combination of Tang et al. and Cowsert. In particular, the combination of these two references does not teach or suggest oligonucleotide compounds capable of specifically hybridizing to a nucleic acid molecule encoding apolipoprotein B (SEQ ID NO: 3), excluding the start codon region as a target region. Moreover, neither Tang et al. nor Cowsert teach or suggest the reduction of apolipoprotein B (SEQ ID NO: 3) mRNA levels of at least 70%. As such, the combination of Tang et al. and Cowsert does not teach all of the limitations of claims 1, 2, 4-14, 20 or 28.

In addition to the foregoing, one of ordinary skill in the art would not reasonably expect to be successful in generating the non-catalytic oligonucleotide compounds encompassed by the instant claims simply because Cowsert purportedly discloses methods for modifying antisense compounds. As set out above, claim 1 recites, in relevant part, that the oligonucleotide compound “demonstrates at least 70% reduction of apolipoprotein B mRNA levels when applied *in vitro* at a concentration of 150nM to HepG2 cells.” Tang et al. in their discussion state that “from the perspective of the empirical inhibition percentage, the results were not very ideal”, and that “the less than ideal inhibition rate was also very likely related to an inadequate AODN concentration”. In contrast to the teachings of Tang et al., Applicants have discovered numerous examples of oligonucleotide compounds that result in reductions of apolipoprotein B mRNA levels of at least 70% (see Table 1). As described in the instant specification, these oligonucleotide compounds are capable of eliciting inhibition of apolipoprotein B mRNA at levels approximately **2.5 times greater** than that achieved by Tang et al., using a concentration of oligonucleotide compound approximately **33 times lower** than that employed by Tang et al. (i.e. the inhibition and concentration required by the instant claims). Even if a skilled artisan were motivated to combine the teachings of Tang et al. with those of Cowsert, s/he would not have a reasonable expectation of success of generating oligonucleotide compounds with significantly higher levels of activity at substantially lower doses, as disclosed and claimed in the instant application.

In view of the foregoing remarks, claims 1, 2, 4-14, 20, and 28 as amended herewith are not obvious over Tang et al. in view of Cowsert. For these reasons, the

references fail to meet the standard of obviousness required under 35 U.S.C. 103(a) and Applicants respectfully request withdrawal of this rejection.

### CONCLUSION

Applicant respectfully requests that claim amendments submitted herewith be entered. In view of the foregoing amendments and remarks, Applicant submits that the application is now in condition for allowance and respectfully requests notification of the same.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

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## **SUMMARY OF INTERVIEW**

### **Identification of Claims Discussed**

All of the pending claims were discussed.

### **Principal Arguments and Other Matters**

Applicants' representatives discussed the pending Office Action and the issues raised by the Examiner with regard to the written description rejection. Applicants' representatives argued that the pending claims met the written description requirements of 35 U.S.C. §112. Applicants' representatives proposed replacing the term "non-cleaving" with "non-catalytic" or "non-enzymatic, and replacing the term "compound" with "oligonucleotide."

### **Results of Interview**

No agreement was reached with the Examiner with regards to the issues presented in the pending Office Action. The Examiner noted that replacing the term "non-cleaving" with "non-catalytic" or "non-enzymatic, and replacing the term "compound" with "oligonucleotide," would obviate the 35 U.S.C. §112, 1<sup>st</sup> paragraph rejection of record.